AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGGGCAGCAGACA
CTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCAGCACTCAGAAGACGGAGGCA
GGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAGTCAGTTGGAAGTCAGCCAGCTTAGACAACA
TGGAGAGCCTGTGCCGAAAGCCACTGGGTAAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTA
CTGC:AAAAAAAAAACCTCAAACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTA
AGCTGATGTGGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGGGCCTCTGGCT
TTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTATAAATTCACCATGAGCTTTAAC
ATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTTTCGATGCTGACACCAATTCAACTGACCTACA
CTCACGGCCTCTGTTTCAACCCCAAGACATTGCCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGA
CTGCTAGGCAATGGGCTGGTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGT
TCCTCCATCTCACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATTCT
CCAAGGACACTGGCCCTATGGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTATTCTCAACATGTTT
GCCAGTGTCTTCCTGCTTACTGCCATTAGCCTGGACCGATGTCTGATAGTACATAAGCCAATCTGGTGCC
AGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTGTGGATGTGTCTGGGTGGTAGCCTTTGTGATGTG
TGTGCCCGTATTTGTATACCGTGATCTGTTCATTATGGACAATCGCAGTATATGTAGATATAATTTTGAT
TCCTCCAGGTCATATGATTATTGGGACTACGTGTACAAACTAAGTCTACCAGAAAGCAATTCTACTGATA
ACTCCACTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGGATTA
CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAGACTCATTCTCTCTA
GATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATGTCCTCACAGCCGCCGTACCCAGCG
GGTTCCTGTTGAAGATCGTAAATCCAATACACTGAACGCTGACGCTTTTCTCTCTGCTCACACAGAACT
TTTCCCTACTGCTTCTAGTGGTCATTTATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACG
TATGACAATCATGTGCCGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGC
CGTTTTTCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCAAGTC
TCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCTGGACTCCATACCAT
CTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGGGGGAAGCTGTGATGTCCTGGGACC
ACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCTTCAACCCTTTCCTGTATGCCCTCTTGGGGAAAGA
CTTTAGGAAGAAAGCAAGACAGTCTATAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCAC
TCTACCAACTGTACCCAAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTG
GCCCTGGGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTAGACA
ATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACATTAAAGATGCAAAAT
TTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATGGGACCAGTGTTTTAACAGGCCTTC
TTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGCTTAGTCTATTCCCATCCCTGACTACACCATGTGC
AATGAATAACTTTTTCATCTGTTTTCAGTATTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTG
CATGGAAGGCTGCTCTTATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAA
GTGATTTTTAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTAGAGT
TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGTTCATGTGAGCA
AGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTTTAGAAGTTGTAGCTTGGAGCTC
(SEQ ID NO:1)

MESFDADTNSTDLHSRPLFQPQDIASMVILGLTCLLGLLGNGLVLWVAGVKMKTTVNTVWFLHLTLADFLCC

LSLPFSLAHLILQGHWPYGLFLCKLIPSIIILNMFASVFLLTAISLDRCLIVHKPIWCQNHRNVRTAFAICGCVWV

VAFVMCVPVFVYRDLFIMDNRSICRYNFDSSRSYDYWDYVYKLSLPESNSTDNSTAQLTGHMNDRSAPSSV

QARDYFWTVTTALQSQPFLTSPEDSFSLDSANQQPHYGGKPPNVLTAAVPSGFPVEDRKSNTLNADAFLSA

HTELFPTASSGHLYPYDFQGDYVDQFTYDNHVPTPLMAITITRLVVGFLVPFFIMVICYSLIVFRMRKTNFTKS

RNKTFRVAVAVVTVFFICWTPYHLVGVLLLITDPESSLGEAVMSWDHMSIALASANSCFNPFLYALLGKDFRK

KARQSIKGILEAAFSEELTHSTNCTQDKASSKRNNMSTDV (SEQ ID NO:2)

FIGURE 1

underlined = deleted in the targeting construct (SEQ ID NO:5)

[ ] = sequence flanking Neo insert in targeting construct (SEQ ID NO:6 and SEQ ID NO:7)

```
AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGG
GCAGCAGACACTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCA
GCACTCAGAAGACGGAGGCAGGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAG
TCAGTTGGAAGTCAGCCAGCTTAGACAACATGGAGAGCCTGT [GCCGAAAGCCACTGGGT
AAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTACTGCAAAAAAAAAACCTC
AAACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTAAGCTGATGT
GGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAA
CTGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGG
GGCCTCTGGCTTTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTAT
AAATTCACCATGAGCTTTAACATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTT
TCGATGCTGACACCAATTCAACTGACCTACACTCACGGCCTCTGTTTCAACCCCAAGACA
TTG] CCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGACTGCTAGGCAATGGGCTG
GTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGTTCCTCCAT
CTCACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATT
CTCCAAGGACACTGGCCCTAT [GGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTAT
TCTCAACATGTTTGCCAGTGTCTTCCTGCTTACTGCCATTAGCCTGGACCGATGTCTGAT
AGTACATAAGCCAATCTGGTGCCAGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTG
TGGATGTGTCTGGGTGGTAGCCTTTGTGATGTGTGTGCCCGTATTTGTATACCGTGATCT
GTTCATTATGGACAATCGCAGTATATGTAGATATAATTTTGATTCCTCCAGGTCATATGA
TTATTGGGACTACGTGT] ACAAACTAAGTCTACCAGAAAGCAATTCTACTGATAACTCCA
CTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGG
ATTACTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAG
ACTCATTCTCTCTAGATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATG
TCCTCACAGCCGCCGTACCCAGCGGGTTTCCTGTTGAAGATCGTAAATCCAATACACTGA
ACGCTGACGCTTTTCTCTCTGCTCACACAGAACTTTTCCCTACTGCTTCTAGTGGTCATT
TATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACGTATGACAATCATGTGC
CGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGCCGTTTT
TCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCA
AGTCTCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCT
GGACTCCATACCATCTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGG
GGGAAGCTGTGATGTCCTGGGACCACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCT
TCAACCCTTTCCTGTATGCCCTCTTGGGGAAAGACTTTAGGAAGAAAGCAAGACAGTCTA
TAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCACTCTACCAACTGTACCC
AAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTGGCCCTG
GGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTA
GACAATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACAT
TAAAGATGCAAAATTTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATG
GGACCAGTGTTTTAACAGGCCTTCTTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGC
TTAGTCTATTCCCATCCCTGACTACACCATGTGCAATGAATAACTTTTTCATCTGTTTTC
AGTATTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTGCATGGAAGGCTGCTCT
TATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAAGTGATT
TTTAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTA
GAGTTTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAG
TGTTCATGTGAGCAAGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTT
TAGAAGTTGTAGCTTGGAGCTC
```

FIGURE 2A

Gene Sequence Structure *

663 bp   Sequence Deleted   859 bp

Size of full-length cDNA: 2658 bp

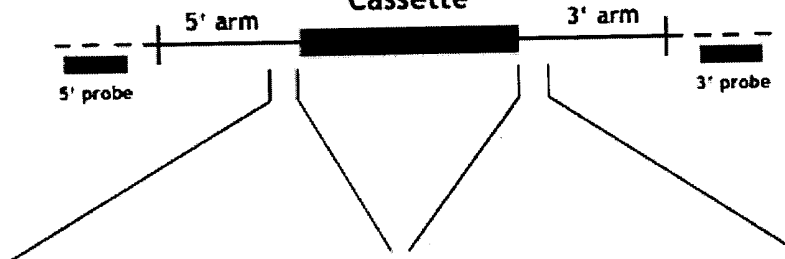**Targeting Vector* (genomic sequence)**

Construct Number: 3036

LacZ-Neo Cassette

5' arm   3' arm

5' probe   3' probe

Arm Length:
5': 3.2 kb
3': 1.8 kb

——— Targeting Vector
– – – – Endogenous Locus

* Not drawn to scale

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5'>CGAGGTTCTGTGAGGGGGGCC
TCTGGCTTTGAGAGGGTGTACCAT
CACATAAGACTCCTAAAAGCACAT
ACTTTTATAAATTCACCATGAGCT
TTAACATCTTCTTTGTCATTTCGC
AGACTGAGCCATGGAGTCTTTCGA
TGCTGACACCAATTCAACTGACCT
ACACTCACGGCCTCTGTTTCAACC
CCAAGACATTG<3'
(SEQ ID NO:3)
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5'>GGCTTGTTCCTGTGCAAACTT
ATCCCATCCATCATTATTCTCAAC
ATGTTTGCCAGTGTCTTCCTGCTT
ACTGCCATTAGCCTGGACCGATGT
CTGATAGTACATAAGCCAATCTGG
TGCCAGAATCATCGAAACGTGAGA
ACCGCCTTCGCCATCTGTGGATGT
GTCTGGGTGGTAGCCTTTGTGATG
TGTGTGCCCGT<3'
(SEQ ID NO:4)
```

FIGURE 2B

necropsy - thymus weight/body weight

Legend:
- 171, Female, F2, N0
- 171, Male, F2, N0

X-axis: Wildtype, Heterozygote, Homozygote

Y-axis: thymus weight(% of total body weight)
0.0, 0.1, 0.2, 0.3, 0.4, 0.5

FIGURE 3